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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,273	03/25/2005	Gautam Vinod Daftary	24439.US	2139

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EXAMINER	
STONE, CHRISTOPHER R	
ART UNIT	PAPER NUMBER
1628	

MAIL DATE	DELIVERY MODE
12/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,273	DAFTARY ET AL.	
	Examiner	Art Unit	
	CHRISTOPHER R. STONE	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27,29-32,34-37,39-41,43-50 and 52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27, 29-32, 34-37, 39-41, 43-50 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed August 13, 2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 27, 29-32, 34-37, 39-41, 43-50 and 52 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Rubinfeld (US 5,602,112) in view of Hausheer et al (US 6,040, 294) and Alexander et al (US 5,227,373).

Rubinfeld teaches a process for preparing a composition comprising adding an antineoplastic drug to a solution of 20% w/v hydroxypropylbetacyclodextrin in water (column 18, Example 1). The cyclodextrin is taught to decrease the toxicity associated with the administration of said antineoplastic drug and nitrogen mustard derivatives are taught be appropriate drugs for use in said process (column 13, lines 46-65 and column 14, lines 3-5). Rubinfeld teaches that the degree of substitution of the cyclodextrin can range from 4 to 10 isopropyl groups per cyclodextrin molecule (4/7 to 10/7 degree of substitution per glucose unit in betacyclodextrin, which comprises about 0.5 to about 1.2, column 16, lines 4-21). Rubinfeld further teaches that the composition may comprise conventional parenteral additives and that the composition is sterilized prior to injection and stored in a sterile container and sealed (column 7, lines 3-19, column 17, lines 1-10). Rubinfeld does not explicitly teach ifosfamide or cyclophosphamide as the particular nitrogen mustard derivative antineoplastic agent or the process further comprising the addition of mesna at the specified concentrations and ratios.

Hausheer et al teaches that ifosfamide and cyclophosphamide are antineoplastic nitrogen mustard derivatives and that the compounds are commonly administered with mesna to decrease the toxicity of said compounds (column 7, lines 47-56 and column 12, lines 57-62).

Alexander et al teaches that ratios of 100:1 to 1:1, ifosfamide to mesna, are appropriate for toxicity reducing dosage forms of ifosfamide (column 4, lines 1-7), that filter sterilization is appropriate for sterilizing said dosage forms (column 4, lines 41-49)

and that 50 mg/ml and 500mg/ml are appropriate concentrations of ifosfamide for said dosage forms (column 6, Example 1 and claims 5-7).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time of the instantly claimed invention to prepare the composition of Rubinfeld using ifosfamide or cyclophosphamide, since these compounds were known nitrogen mustard derivatives, to further add mesna for its known toxicity reducing activity, and to make up the volume of the solution with water so that the final concentrations/ratios of composition components meet the values of claims 27, 34-36, 39-41, 43 and 44, since said values fall within the ranges, noted above, to be appropriate for preparing oxazaphosphorine dosage forms, thus resulting in the instantly claimed composition/process with a reasonable expectation of success.

Additionally it would have been prima facie obvious to one of ordinary skill in the art at the time of the instantly claimed invention to administer the sterile composition to a patient suffering from a malignant disease (i.e. cancer), since, as noted above, ifosfamide and cyclophosphamide were known antineoplastic agents (i.e. agents useful in the treatment of cancer), thus resulting in the practice of the instantly claimed invention with a reasonable expectation of success.

Response to Arguments

Applicant alleges that one of ordinary skill in the art would not assume that a formulation of cyclodextrin and ifosfamine or cyclophosphamide would lower ifosfamide or cyclophosphamide induced toxicity. This is found unpersuasive because Rubinfeld demonstrates the toxicity reducing effects of cyclodextrin on structurally distinct

compounds (Examples I-VI) and further cites numerous references in which cyclodextrin complexes decrease the side effects associated with a particular drug and increase drug stability (columns 3 and 4). Furthermore, as noted above, Rubinfeld expressly teaches nitrogen mustard derivatives, a class of drug of which ifosfamine and cyclophosphamide are members, as appropriate for cyclodextrin complex formation to decrease known toxicities, providing one of ordinary skill in the art with a reasonable expectation of success in practicing the instantly claimed method. Applicant argues that Alexander teaches away aqueous compositions of ifosfamide in favor of lyophilized formulations (p. 9 of the Reply filed August 13, 2009). This is found unpersuasive because Alexander does not teach away from the instantly claimed invention, i.e. oxazaphosphorine compositions stabilized by cyclodextrin complexation, that is, none of the comparative examples of Alexander are prepared with cyclodextrin, which as noted above, was known to increase stability and decrease toxicity in drug formulations. Applicant argues that the optimization of the concentration of composition components would not have been obvious to one of ordinary skill in the art since said concentrations were not recognized as a results effective variable. This is found unpersuasive because Rubinfeld expressly teaches that the relative amounts of composition components, e.g. cyclodextrin and cytotoxic compound, will vary dependent upon the relative toxicity of the compound and the effect of cyclodextrin on the compound (see column 16, lines 22-55), thus identifying the relative concentrations of components as a results effective parameter and providing motivation to one of ordinary skill in the art to optimize said parameter.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER R. STONE whose telephone number is (571)270-3494. The examiner can normally be reached on Monday-Thursday, 7:30am-4:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CRS

/Brandon J Fetterolf/
Primary Examiner, Art Unit 1642